## Remarks

Claims 2, 21, 22, and 27-29 were pending; new claim 30 is presented. As a result, claims 2, 21, 22, and 27-30 are pending. Support for claim 30 and the other pending claims is discussed below.

*The Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph*

Claims 2, 21, 22, 27, 28, and 29 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is respectfully traversed.

Claims 2 and 27

Definiteness of claim language is analyzed, not in a vacuum, but in light of (1) the content of the specification, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one of ordinary skill in the pertinent art. M.P.E.P. § 2173.02. "A claim is not 'indefinite' simply because it is hard to understand when viewed without benefit of the specification." *S3 Inc. v. nVidia Corp.*, 259 F.3d 1364, 1369 (Fed. Cir. 2001).

Claim 27 recites an isolated nucleic acid molecule encoding residues 10,432 to 22,152 of SEQ ID NO:5 or a fragment of residues 10,432 to 22,152 of SEQ ID NO:5; wherein the isolated nucleic acid molecule is an expression vector and is adapted to express in a cell residues 10,432 to 22,152 of SEQ ID NO:5 or a fragment of residues 10,432 to 22,152 of SEQ ID NO:5; wherein the fragment of residues 10,432 to 22,152 of SEQ ID NO:5 is an antigenic fragment that can be used to make monoclonal antibodies that specifically recognize CA125.

The Examiner stated that the claim is unclear because it is unclear if the claims encompass nucleic acids that encode and express fragments larger than residues 10,432 to 22,152 of SEQ ID NO:5.

The claims are clear. Reciting that a nucleic acid molecule encodes certain polypeptide residues does not exclude the possibility that it also encodes other residues. In fact, the Examiner implicitly acknowledges that claim 27 covers nucleic acid molecules that encode residues in addition to residues 10,432 to 22,152 of SEQ ID NO:5,

since he acknowledges that the claim language does not exclude that. If there were any doubt about that broader interpretation of claim 27, it would be dispelled by dependent claim 2, which recites the isolated nucleic acid molecule of claim 27 comprising the sequence of SEQ ID NO:4, since SEQ ID NO:4 encodes all of SEQ ID NO:5, not just residues 10,432 to 22,152 of SEQ ID NO:5.

Claims 21, 22, 28, 29, and 30

Claim 28 recites an isolated nucleic acid molecule encoding CA125 (SEQ ID NO:5) or a fragment thereof; wherein the isolated nucleic acid molecule is an expression vector and is adapted to express in a cell CA125 (SEQ ID NO:5) or a fragment thereof; wherein the fragment thereof is an antigenic fragment that can be used to make monoclonal antibodies that specifically recognize CA125 (SEQ ID NO:5); wherein the isolated nucleic acid molecule encodes residues 1 to 10,431 of SEQ ID NO:5 or a fragment of residues 1 to 10,431 of SEQ ID NO:5.

The Examiner stated that it is unclear if the nucleic acid is only required to encode residues 1 to 10,431 of SEQ ID NO:5 or a fragment of residues 1 to 10,431 of SEQ ID NO:5 and not necessarily express them.

Claim 28 is clear. It recites that the isolated nucleic acid molecule is adapted to express SEQ ID NO:5 or a fragment thereof. It also recites that the isolated nucleic acid molecule encodes residues 1 to 10,431 of SEQ ID NO:5 or a fragment of residues 1 to 10,431 of SEQ ID NO:5. It does not recite that the isolated nucleic acid molecule is adapted to express residues 1 to 10,431 of SEQ ID NO:5 or a fragment of residues 1 to 10,431 of SEQ ID NO:5 and therefore the nucleic acid does not necessarily express residues 1 to 10,431 of SEQ ID NO:5 or a fragment of residues 1 to 10,431 of SEQ ID NO:5.

The Examiner also stated that it is unclear if polynucleotides expressing fragments larger than residues 1 to 10,431 of SEQ ID NO:5 are encompassed by the claim. Again, as with claim 27 discussed above, reciting that a nucleic acid molecule encodes certain polypeptide residues does not exclude the possibility that it also encodes other residues. Therefore, claim 28 encompasses polynucleotides expressing fragments larger than residues 1 to 10,431 of SEQ ID NO:5.

Accordingly, claims 2, 21, 22, and 27-30 are definite, and Applicants respectfully request withdrawal of the rejection of claims 2, 21, 22, and 27-29 as indefinite under 35 U.S.C. § 112, second paragraph.

*The Rejection of the Claims Under 35 U.S.C. § 112, First Paragraph*

Claims 21, 22, 27, 28, and 29 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. This rejection is respectfully traversed.

The Guidelines for Examination of Patent Applications under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement (66 Fed Register 1099) state: "While there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure" (*Id.* at p. 1105, column 1).

The Board of Patent Appeals and Interferences in *Ex parte Parks*, 30 U.S.P.Q.2d 1234, 1236 (Bd. Pat. App. & Int. 1994) stated:

> Adequate description under the first paragraph of 35 U.S.C. 112 does not require *literal* support for the claimed invention. . . . Rather, it is sufficient if the originally filed disclosure would have conveyed to one having ordinary skill in the art that an appellant had possession of the concept of what is claimed. (Emphasis added.)

The Court of Customs and Patent Appeals held regarding compliance with the written description requirement:

> [T]he disclosure in question must be read in light of the knowledge possessed by those skilled in the art, and that knowledge can be established by affidavits of fact composed by an expert, and by reference to patents and publications available to the public prior to appellant's filing date. *In re Lange*, 644 F.2d 856, 863 (C.C.P.A. 1981).

Thus, the test for compliance with the written description requirement is whether one of ordinary skill in the art would recognize based on the originally filed disclosure that the inventors were in possession of the concept of what is claimed.

Parent application serial no. 09/965,738 at page 32, lines 10-11 discloses "Antibodies to CA125 epitopes or newly described potential epitopes." Page 31, lines 27-28 of application serial no. 09/965,738 discloses "recombinant antigen containing the

CA125 epitopes or other domains." And page 31, line 30 of application serial no. 09/965,738 discloses "recombinant CA125 epitope domain or other domains or . . . peptides derived from these domains." "Peptides derived from" CA125 "domains", can only be fragments of CA125. The text at page 31, lines 29-30, and page 32, lines 10-11, is not limited to epitopes and peptides of a particular portion of CA125. Instead it says "epitope domains or other domains" and "newly discovered potential epitopes," which indicates that peptide fragments of the entire molecule is contemplated – parts of the molecule bound by existing antibodies and other parts, "newly discovered potential epitopes," to which antibodies can be raised.

The phrases quoted above show that one of ordinary skill in the art would recognize that Applicants were in possession of an expression vector: "Recombinant" peptides, domains, and proteins must be those produced from recombinant nucleic acid. A recombinant nucleic acid that expresses a peptide or protein is an expression vector. The phrases quoted additionally show that one of ordinary skill in the art would recognize that Applicants were in possession of the concept of expressing antigenic fragments of the entire CA125 molecule disclosed: It discloses "recombinant CA125 epitope domain or other domains or . . . peptides derived from these domains." "[E]pitope domain or other domains" contemplates domains that hold currently recognized epitopes and "other domains," which must refer to the rest of the molecule. It discloses "peptides derived from" the "epitope domains or other domains," so that is a disclosure of peptides covering the whole CA125 molecule. Plainly one of ordinary skill in the art would recognize that Applicants were in possession of an isolated nucleic acid that is an expression vector encoding and expressing any fragment of CA125 that can be used to make antibodies that recognize the fragment.

In addition, the specific fragment recited in claim 27, resides 10,432 to 22,152 of SEQ ID NO:5, is disclosed in parent application serial no. 09/965,738, filed September 27, 2001, as SEQ ID NO:162.

Thus, claim 27 is fully supported by parent application serial no. 09/965,738, filed September 27, 2001.

Claims 2, 21, 22, 28, 29, and 30 are supported by parent international application no. PCT/US02/11734, filed April 12, 2002, which discloses as its SEQ ID NO:310 the

amino terminal extension of CA125 that is residues 1-10,431 of SEQ ID NO:5. It also discloses specifically the fragment constituting residues 1-10,427 of SEQ ID NO:5, e.g., in its claim 1, part (b).

The Examiner has argued only that the exact wording of the present claims is not found in the originally filed specification of the present application. But that is not the test for compliance with the written description requirement. The test is whether one of ordinary skill in the art would recognize based on the originally filed disclosure that the inventors were in possession of the concept of what is claimed. There is no doubt the inventors were in possession of the concept of expression vectors to express recombinant polypeptides comprising antigenic fragments of any part of CA125, which was disclosed to comprise residues 10,432 to 22,152 of SEQ ID NO:5 in parent application serial no. 09/965,738, filed September 27, 2001 (SEQ ID NO:162 of that application) and to additionally comprise residues 1-10,431 of SEQ ID NO:5 in parent international application no. PCT/US02/11734, filed April 12, 2002. The nucleic acid of SEQ ID NO:4 is also disclosed in parent international application no. PCT/US02/11734, filed April 12, 2002. Accordingly, claim 27 is supported by parent application serial no. 09/965,738, filed September 27, 2001, and claims 2, 21, 22, 28, and 29 are supported by parent international application no. PCT/US02/11734, filed April 12, 2002.

Since the parent applications clearly convey the concept of expression vectors expressing any antigenic fragment of CA125 as a recombinant polypeptide, and disclose that CA125 comprises residues 10,432 to 22,152 of the present SEQ ID NO:5 in parent application serial no. 09/965,738, filed September 27, 2001, and that CA125 additionally comprises residues 1-10,431 of SEQ ID NO:5 in parent international application no. PCT/US02/11734, filed April 12, 2002, claims 2, 21, 22, and 27-29 satisfy the written description requirement. This also establishes that claim 27 has a priority date of at least September 27, 2001, and claims 2, 21, 22, 28, and 29 have a priority date of at least April 12, 2002.

In view of these remarks, Applicants request withdrawal of the rejection of claims 2, 21, 22, and 27-29 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

*The Rejection of the Claims Under 35 U.S.C. § 102(b)*

Claim 27 was rejected under 35 U.S.C. § 102(b) as being anticipated by Yin and Lloyd (*J. Biol. Chem.*, July 20, 2001, 276:27371-27375). This rejection is respectfully traversed.

Claim 27 has a priority date of at least September 27, 2001, since it is supported by parent application serial no. 09/965,738, as discussed above. Yin and Lloyd was published July 20, 2001, less than 1 year before this. Thus, it is not a reference under 35 U.S.C. § 102(b). Provisional patent application 60/299,380, which was filed June 19, 2001, before Yin and Lloyd, also supports claim 27 and therefore antedates Yin and Lloyd. But Applicants will not argue that here. Instead, Applicants point out that provisional patent application serial no. 60/299,380, unarguably discloses reduction to practice of so much of the invention as is disclosed in Yin and Lloyd, and thus it removes Yin and Lloyd as prior art.

> All the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show. When he has done that he has disposed of the reference.
>
> . . . In the case of a reference, it is fundamental that it is valid only for what it discloses and if the applicant establishes priority with respect to that disclosure, and there is no statutory bar, it is of no effect at all.
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> *In re Stempel*, 241 F.2d 755, 113 U.S.P.Q. 77 (Ct. Customs & Pat. Appeals 1957).

Yin and Lloyd (*J. Biol. Chem.*, July 20, 2001, 276:27371-27375) states that the authors isolated a 5797-base pair sequence containing a stop codon but no clear 5' initiation sequence (abstract). And it is dated July 20, 2001. The alignment the Examiner shows, however, is with Genbank locus AF361486, which is 21,112 bp (not 5797 bp) and states that it was updated on Sept. 8, 2003.

The protein sequence Yin and Lloyd discloses is homologous with portions of the multiple repeat domain and the carboxy terminal domain of the present SEQ ID NO:5 from residues 12,070 to 22,152 of SEQ ID NO:5.[1]

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[1] The Yin and Lloyd *J. Biol. Chem.* paper does not disclose the sequence of the nucleic acid isolated. It states that the nucleic acid sequence they found produced a "deduced amino acid sequence of 1890 amino acids (Fig. 3)" (page 27372 second column) and it shows the deduced amino acid sequence in Fig. 3. Alignment of residues

Provisional patent application serial no 60/299,380, filed June 19, 2001, discloses SEQ ID NOS:34, 36, and 38 in Tables 14, 16, and 18 (of the provisional patent application) to be the amino terminal domain, repeat domain, and carboxy terminal domain of CA125 and discloses the nucleic acid sequences encoding those protein sequences. Together those protein sequences make up residues 10,432-22,152 of SEQ ID NO:5 as is recited in claim 27. It also discloses expressing fragments of these sequences to produce recombinant polypeptides. Pages 6-7 of provisional patent application serial no. 60/299,380 disclose isolated nucleic acids and fragments of the nucleic acids isolated, and expressing isolated nucleic acids from vectors. Page 2, first line of the Summary of provisional patent application serial no. 60/299,380 discloses isolating portions of the CA125 gene. Page 3, lines 5-10 and page 4, line 3 of provisional patent application serial no. 60/299,380 discloses use of recombinant domains, such as individual repeat units, of CA125. Page 3, lines 11-18 of provisional patent application serial no. 60/299,380 discloses recombinant domains of CA125 encompassing epitope binding sites for murine antibodies, and use of the recombinant molecules as vaccines or to stimulate patients' immune systems. Thus, Applicant was in possession of more of the CA125 protein and nucleic acid sequence than is disclosed by Yin and Lloyd before the publication of Yin and Lloyd, and had constructively reduced to practice with the provisional patent application isolated nucleic acids expressing these sequences and fragments of them before the publication date of Yin and Lloyd.

Yin and Lloyd (*J. Biol. Chem.*, July 20, 2001, 276:27371-27375) states that the authors isolated a 5797-base pair sequence containing a stop codon but no clear 5' initiation sequence (abstract). And it is dated July 20, 2001. Applicants must point out,

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1-100 of the sequence shown in the top portion of Fig. 3 of Yin and Lloyd with the present SEQ ID NO:5 shows imperfect homology with several sequences in the multiple repeat region from residues 12,070 to 21,868 of SEQ ID NO:5. The best homology begins with residue 13721 of SEQ ID NO:5.

Alignment of the sequence beginning with FNFWSS in the middle portion of Fig. 3 with SEQ ID NO:5 produced imperfect homology also with several segments of the multiple repeat domain of SEQ ID NO:5 between residues 12,070 and 21,868 of SEQ ID NO:5. The best homology begins at residue 15,004 of SEQ ID NO:5.

Alignment of the last line of sequence in Fig. 3, beginning with VLVDGYSPN with SEQ ID NO:5 produced alignment beginning at residues 22,076 of SEQ ID NO:5, in the carboxy terminal domain.

though, that the alignment the Examiner shows, is with Genbank locus AF361486, which is 21,112 bp (not 5797 bp) and states that it was updated on Sept. 8, 2003.

Applicant previously submitted the revision history of AF361486 and AF361486 version 1 GI:14971109. The revision history shows that version GI:14971109 is the earliest version of AF361486 and was submitted on July 20, 2001. In the version submitted on July 20, 2001, AF361486 only had 5797 nucleotides, the same as Yin and Lloyd. The next revision of AF361486 was on Aug. 26, 2003. Version GI:14971109 encodes an 1890-amino-acid protein that is homologous to the carboxy terminal 1890 amino acid residues of the present SEQ ID NO:5 and appears to be the protein sequence disclosed in Yin and Lloyd. The 21,112 bp sequence of the present AF361486 was only submitted on September 8, 2003. Thus, the alignment the Examiner has used to reject claim 27 is not with the disclosure of Yin and Lloyd on July 21, 2001, but is with a Genbank submission made on September 8, 2003, long after the priority date of claim 27.

The Examiner has chosen to simply ignore these facts, and states wrongly that the publication date of the updated AF3616486 that he uses for alignment is July 20, 2001, rather than its actual publication date of September 8, 2003 (page 13 of the Office Action mailed August 8, 2008).

Thus, Yin and Lloyd does not anticipate any of the present claims.

Claim 27 was rejected under 35 U.S.C. § 102(b) as being anticipated by O'Brien et al. (Tumor Biology, 2001 Nov-Dec; 22(6):348-366) as evidenced by O'Brien et (Tumor Biology 2002 May-June; 23(3):154-169). This rejection is respectfully traversed.

As demonstrated above, claim 27 is fully supported by parent application serial no. 09/965,738, filed September 27, 2001, before the publication dates of either of the O'Brien et al. references cited.

Claims 21, 22, 27, and 28 were rejected under 35 U.S.C. § 102(b) as being anticipated by WO 2002/68579 (Venter et al. 6 September 2002). This rejection is respectfully traversed.

As demonstrated above, claim 27 is fully supported by parent application serial no. 09/965,738, filed September 27, 2001, and claims 2, 21, 22, and 28-30 are fully

supported by parent international application no. PCT/US02/11734, filed April 12, 2002. These dates are before 6 September 2002, so WO 2002/68579 is not prior art to any of the present claims.

Claim 27 was rejected under 35 U.S.C. § 102(b) as being anticipated by WO 2001/51513 (Algate et al. 19 July 2001). This rejection is respectfully traversed.

The Examiner cites only page 2, lines 11-15 of Algate, which states that the invention provides polynucleotides that encode a polypeptide and expression vectors. It does not disclose any amino acid or nucleotide sequence. In Appendix 3 of the Office Action, the Examiner shows an alignment of a nucleic acid showing that it encodes a polypeptide homologous to amino acid residues 21897 to 22065 of SEQ ID NO:5. (The numbering on the upper line of Appendix 3 is 2747 to 2914, but the amino acid residues are actually residues 21898 to 22065 of SEQ ID NO:5.) The Examiner does not cite the page or line number or SEQ ID NO where the nucleic acid sequence shown in Appendix 3 allegedly appears in Algate.

The Examiner has the initial burden to establish the basis for an anticipation rejection under 35 U.S.C. § 102. The Examiner must point with particularity to where the reference discloses information that anticipates the invention. "[I]t is incumbent upon the Patent Office . . . to set forth clearly why it regards a claim to be anticipated . . . ." *In re Mullin*, 481 F.2d 133, 1336, 179 U.S.P.Q. 97, 100 (Ct. Customs & Pat. Appeals 1973). Here the Examiner has not met this burden. He has made a bare assertion that Algate discloses some nucleic acid sequence that is shown as encoding a polypeptide homologous with residues in SEQ ID NO:5 in Appendix 3 of the Office Action mailed August 8, 2008. He has not cited where in Algate this sequence is allegedly disclosed.

Accordingly, the rejection must be withdrawn.

If the sequence shown in Appendix 3 of the Office Action is actually disclosed in Algate, it encodes a protein sequence homologous to residues 21898 to 22065 of SEQ ID NO:5. This sequence is also disclosed in the priority U.S. provisional patent application no. 60/299,380, which was filed June 19, 2001. As is discussed above, U.S. provisional patent application no. 60/299,380 discloses nucleic acids encoding residues 10,432-22,152 of SEQ ID NO:5, and expression vectors encoding and expressing that protein

sequence and fragments thereof. Thus, it establishes " priority with respect to so much of the claimed invention as the reference happens to show"[2] and therefore removes Algate as prior art under 35 U.S.C. § 102(a) as well as 35 U.S.C. § 102(b).

In addition, a Declaration under 37 C.F.R. § 1.131 by the Applicants is submitted herewith, which establishes reduction to practice of so much of the invention as is alleged to be disclosed by Algate before the filing date of Algate of January 16, 2001. The Rule 131 Declaration is accompanied by an Invention Disclosure form and laboratory notebook pages dated before January 16, 2001 that establish the Applicants

> were in possession of and had reduced to practice in the United States before January 16, 2001, recombinant nucleic acids encoding residues 21898 to 22065 of SEQ ID NO:5 and surrounding sequences; and we were in possession of and had reduced to practice in the United States before January 16, 2001, an expression vector that expressed a recombinant fragment of CA125 that was recognized by a monoclonal antibody (M11) that recognizes CA125 and therefore could by used to make monoclonal antibodies that specifically recognize CA125. (Rule 131 Declaration, paragraph 8).

In view of the remarks herein, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 102(b) of Claim 27 over Yin and Lloyd, claim 27 over O'Brien et al. (Tumor Biology, 2001 Nov-Dec; 22(6):348-366) as evidenced by O'Brien et (Tumor Biology 2002 May-June; 23(3):154-169), claims 21, 22, 27, and 28 over WO 02/68579 (Venter et al.), and claim 27 over WO 2001/51513 (Algate et al.).

*Double Patenting*

Claims 2, 21, 22, 27, 28, and 29 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 48-50 and 52-55 of copending application no. 11/975,668 in view of U.S. Patent No. 4,889,806 and Sambrook et al. (Molecular Cloning, A Laboratory Manual, Cold Spring Harbor, 1989, pp. 16.3-36).

This is a provisional rejection. It is inapplicable unless the claims of copending application no. 11/975,668 issue before the claims of the present application. Applicants

[2] *In re Stempel*, 241 F.2d 755, 113 U.S.P.Q. 77 (Ct. Customs & Pat. Appeals 1957).

will address the rejection upon notice of allowance of the claims in copending application no. 11/975,668.

*Conclusion*

Applicants believe the claims are in condition for allowance, and notification of allowance is respectfully requested. The Examiner is invited to telephone Applicants' attorney (651-207-8270) to facilitate prosecution of this application.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient first class postage, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this day December 8, 2008.

Hugh McTavish